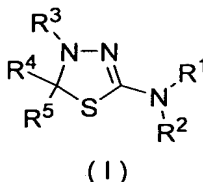


What is claimed is:

1. A mitotic kinesin Eg5 inhibitor which comprises a thiadiazoline derivative represented by the general formula (I) or a pharmacologically acceptable salt thereof as an active ingredient:



<wherein R<sup>1</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group;

R<sup>2</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group,

-C(=W)R<sup>6</sup> [wherein W represents an oxygen atom or a sulfur atom, and R<sup>6</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, -NR<sup>7</sup>R<sup>8</sup> (wherein R<sup>7</sup> and R<sup>8</sup> are the same or different and each represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, or R<sup>7</sup> and R<sup>8</sup> are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group), -OR<sup>9</sup> (wherein R<sup>9</sup> represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group) or -SR<sup>10</sup> (wherein R<sup>10</sup> has the same meaning as that of the aforementioned R<sup>9</sup>)], -NR<sup>11</sup>R<sup>12</sup> {wherein R<sup>11</sup> and R<sup>12</sup> are the same or different and each represents a hydrogen atom, substituted or unsubstituted

lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group,  $-C(=O)R^{13}$  [wherein  $R^{13}$  represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group,  $-NR^{14}R^{15}$  (wherein  $R^{14}$  and  $R^{15}$  are the same or different and each represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, or  $R^{14}$  and  $R^{15}$  are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group),  $-OR^{16}$  (wherein  $R^{16}$  has the same meaning as that of the aforementioned  $R^9$ ), or  $-SR^{17}$  (wherein  $R^{17}$  has the same meaning as that of the aforementioned  $R^9$ )], or

$R^{11}$  and  $R^{12}$  are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group}, or  $-SO_2R^{18}$  (wherein  $R^{18}$  represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group), or

$R^1$  and  $R^2$  are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group,

$R^3$  represents a hydrogen atom, or  $-C(=Z)R^{19}$  [wherein  $Z$  represents an oxygen atom or a sulfur atom, and  $R^{19}$  represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group,

$-NR^{20}R^{21}$  (wherein  $R^{20}$  and  $R^{21}$  are the same or different and each represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, or  $R^{20}$  and  $R^{21}$  are combined together with the

adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group), -OR<sup>22</sup> (wherein R<sup>22</sup> represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group), or -SR<sup>23</sup> (wherein R<sup>23</sup> has the same meaning as that of the aforementioned R<sup>22</sup>)],

R<sup>4</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, and

R<sup>5</sup> represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, or

R<sup>4</sup> and R<sup>5</sup> are combined together to represent -(CR<sup>25A</sup>R<sup>25B</sup>)<sub>m1</sub>Q(CR<sup>25C</sup>R<sup>25D</sup>)<sub>m2</sub> {wherein Q represents a single bond, substituted or unsubstituted phenylene or cycloalkylene, m1 and m2 are the same or different and each represents an integer of from 0 to 4, with the proviso that m1 and m2 are not 0 at the same time, R<sup>25A</sup>, R<sup>25B</sup>, R<sup>25C</sup> and R<sup>25D</sup> are the same or different and each represents a hydrogen atom, halogen, substituted or unsubstituted lower alkyl, -OR<sup>26</sup> [wherein R<sup>26</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, -CONR<sup>27</sup>R<sup>28</sup> (wherein R<sup>27</sup> and R<sup>28</sup> are the same or different and each represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, or R<sup>27</sup> and R<sup>28</sup> are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group), -SO<sub>2</sub>NR<sup>29</sup>R<sup>30</sup> (wherein R<sup>29</sup> and R<sup>30</sup> have the same meanings as those of the aforementioned R<sup>27</sup> and R<sup>28</sup>, respectively), or -COR<sup>31</sup> (wherein R<sup>31</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or

a substituted or unsubstituted heterocyclic group)], -NR<sup>32</sup>R<sup>33</sup> [wherein R<sup>32</sup> and R<sup>33</sup> are the same or different and each represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, -COR<sup>34</sup> (wherein R<sup>34</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, substituted or unsubstituted lower alkoxy, substituted or unsubstituted aryloxy, amino, substituted or unsubstituted lower alkylamino, substituted or unsubstituted di-(lower alkyl)amino, or substituted or unsubstituted arylamino), or -SO<sub>2</sub>R<sup>35</sup> (wherein R<sup>35</sup> represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group)], or -COOR<sup>36</sup> (wherein R<sup>36</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group), or R<sup>25A</sup> and R<sup>25B</sup>, or R<sup>25C</sup> and R<sup>25D</sup> are combined together to represent an oxygen atom, and when m1 or m2 is an integer of 2 or above, any of R<sup>25A</sup>, R<sup>25B</sup>, R<sup>25C</sup> and R<sup>25D</sup> may be the same or different, and any two of R<sup>25A</sup>, R<sup>25B</sup>, R<sup>25C</sup> and R<sup>25D</sup> which are bound to the adjacent two carbon atoms may be combined to form a bond}>.

2. The mitotic kinesin Eg5 inhibitor according to claim 1, wherein R<sup>2</sup> is -C(=W)R<sup>6</sup> (wherein W and R<sup>6</sup> have the same meanings as those mentioned above, respectively).

3. The mitotic kinesin Eg5 inhibitor according to claim 2, wherein R<sup>6</sup> is substituted or unsubstituted lower alkyl.

4. The mitotic kinesin Eg5 inhibitor according to any one of claims 1 to 3, wherein R<sup>3</sup> is -C(=Z)R<sup>19</sup> (wherein Z and R<sup>19</sup> have the same meanings as those mentioned above, respectively).

5. The mitotic kinesin Eg5 inhibitor according to claim 4, wherein R<sup>19</sup> is substituted or unsubstituted lower alkyl.

6. The mitotic kinesin Eg5 inhibitor according to any one of claims 1 to 5, wherein R<sup>5</sup> is substituted or unsubstituted aryl, or a substituted or unsubstituted aromatic heterocyclic group.

7. The mitotic kinesin Eg5 inhibitor according to any one of claims 1 to 5, wherein R<sup>5</sup> is substituted or unsubstituted aryl.

8. The mitotic kinesin Eg5 inhibitor according to any one of claims 1 to 7, wherein R<sup>4</sup> is substituted or unsubstituted lower alkyl, or -(CH<sub>2</sub>)<sub>n</sub>NHSO<sub>2</sub>R<sup>24</sup> (wherein n represents 1 or 2, and R<sup>24</sup> represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, amino, lower alkylamino, or di-(lower alkyl)amino).

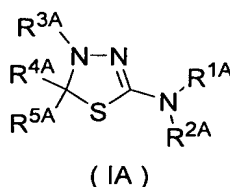
9. The mitotic kinesin Eg5 inhibitor according to any one of claims 1 to 5, wherein R<sup>4</sup> and R<sup>5</sup> are combined together to represent -(CR<sup>25A</sup>R<sup>25B</sup>)<sub>m1</sub>Q(CR<sup>25C</sup>R<sup>25D</sup>)<sub>m2</sub> (wherein R<sup>25A</sup>, R<sup>25B</sup>, R<sup>25C</sup>, R<sup>25D</sup>, m<sub>1</sub>, m<sub>2</sub> and Q have the same meanings as those mentioned above, respectively).

10. The mitotic kinesin Eg5 inhibitor according to claim 9, wherein Q is substituted or unsubstituted phenylene.

11. The mitotic kinesin Eg5 inhibitor according to any one of claims 1 to 10, wherein R<sup>1</sup> is a hydrogen atom.

12. The mitotic kinesin Eg5 inhibitor according to any one of claims 1 to 11, wherein W and Z are oxygen atoms.

13. A thiadiazoline derivative represented by the general formula (IA) or a pharmacologically acceptable salt thereof:



<wherein R<sup>1A</sup> represents a hydrogen atom,

R<sup>2A</sup> represents a hydrogen atom or -COR<sup>6A</sup> (wherein R<sup>6A</sup> represents substituted or unsubstituted lower alkyl), or R<sup>1A</sup> and R<sup>2A</sup> are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group,

R<sup>3A</sup> represents -COR<sup>19A</sup> (wherein R<sup>19A</sup> represents substituted or unsubstituted lower alkyl),

R<sup>4A</sup> represents -(CH<sub>2</sub>)<sub>p</sub>NR<sup>4AA</sup>R<sup>4AB</sup> [wherein p represents 1 or 2, and R<sup>4AA</sup> and R<sup>4AB</sup> are

the same or different and each represents a hydrogen atom, lower alkyl or cycloalkyl (with the proviso that when  $R^{2A}$  is  $-COR^{6A}$ ,  $R^{6A}$  and  $R^{19A}$  are tert-butyl and  $R^{5A}$  is phenyl,  $R^{4AA}$  and  $R^{4AB}$  are not methyl at the same time)],  $-(CH_2)_pNR^{4AD}COR^{4AC}$  (wherein  $p$  has the same meaning as that mentioned above,  $R^{4AC}$  represents a hydrogen atom, lower alkyl or lower alkoxy, and  $R^{4AD}$  represents a hydrogen atom or lower alkyl), or  $-(CH_2)_pNHSO_2R^{24A}$  {wherein  $p$  has the same meaning as that mentioned above,  $R^{24A}$  represents  $-(CH_2)_qNR^{24AA}R^{24AB}$  [wherein  $q$  represents an integer of from 0 to 5, and  $R^{24AA}$  and  $R^{24AB}$  are the same or different and each represents a hydrogen atom, substituted or unsubstituted lower alkyl or cycloalkyl (with the proviso that when  $R^{2A}$  is  $-COR^{6A}$ ,  $R^{6A}$  is tert-butyl and  $R^{19A}$  is methyl or tert-butyl, neither of  $R^{24AA}$  and  $R^{24AB}$  is methyl, and if one of  $R^{24AA}$  and  $R^{24AB}$  is a hydrogen atom in this case, the other is not ethyl or hydroxyethyl)], 3-chloropropyl, 3-azidopropyl or lower alkenyl (with the proviso that when  $R^{2A}$  is  $-COR^{6A}$ ,  $R^{6A}$  is tert-butyl and  $R^{19A}$  is methyl or tert-butyl,  $R^{24A}$  is not vinyl)}, and  $R^{5A}$  represents substituted or unsubstituted aryl or a substituted or unsubstituted aromatic heterocyclic group>.

14. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 13, wherein  $R^{5A}$  is substituted or unsubstituted aryl.

15. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 13, wherein  $R^{5A}$  is phenyl.

16. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 13 to 15, wherein  $R^{2A}$  is  $COR^{6A}$ , and  $R^{6A}$  is unsubstituted lower alkyl.

17. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 13 to 15, wherein  $R^{2A}$  is  $COR^{6A}$ , and  $R^{6A}$  is tert-butyl.

18. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 13 to 17, wherein  $R^{19A}$  is unsubstituted lower alkyl.

19. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 13 to 17, wherein  $R^{19A}$  is tert-butyl.

20. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 13 to 19, wherein  $R^{4A}$  is  $-(CH_2)_pNR^{4AA}R^{4AB}$

(wherein p, R<sup>4AA</sup> and R<sup>4AB</sup> have the same meanings as those mentioned above, respectively).

21. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 13 to 19, wherein R<sup>4A</sup> is  $-(CH_2)_pNR^{4AD}COR^{4AC}$  (wherein p, R<sup>4AC</sup> and R<sup>4AD</sup> have the same meanings as those mentioned above, respectively).

22. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 13 to 19, wherein R<sup>4A</sup> is  $-(CH_2)_pNHSO_2R^{24A}$  (wherein p and R<sup>24A</sup> have the same meanings as those mentioned above, respectively).

23. A medicament which comprises the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 13 to 22 as an active ingredient.

24. A mitotic kinesin Eg5 inhibitor which comprises the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 13 to 22 as an active ingredient.

25. A method for inhibiting a mitotic kinesin Eg5 which comprises administering an effective amount of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 1 to 12.

26. A method for inhibiting a mitotic kinesin Eg5 which comprises administering an effective amount of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 13 to 22.

27. Use of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 1 to 12 for the manufacture of a mitotic kinesin Eg5 inhibitor.

28. Use of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 13 to 22 for the manufacture of a mitotic kinesin Eg5 inhibitor.